

## **B. Claim Rejections under 35 U.S.C. § 112**

Claims 10-13 are rejected under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite, because Claim 13, *inter alia*, does not indicate with what “said expression of said gene in said plurality of samples” is to be compared. Applicants respectfully disagree. However, for the purpose of expediting the issuance of the claims, Applicants have amended Claim 13.

The Examiner further alleges that the language “using the expression of said at least three maintenance genes” does not apprise one of skill in the art as to how the “expression of said at least three maintenance genes” is to be “used” in the comparing step in the practice of the claimed method. Applicants have replaced the word “using” with “with,” and the claim is now within the acquaintance of one skilled in the art. Therefore, this rejection of Claims 10-13 is obviated.

Claims 10-13 are considered allegedly indefinite over the recitation of the list of maintenance genes set forth in claim 13, since the list comprises mRNA and protein names, rather than gene names. Applicants respectfully disagree with the Examiner. Claims need only reasonably apprise those skilled in the art for their scope and be as precise as the subject matter permits. It is thus readily apparent to a person skilled in the art that both protein and mRNA names may be used to define a gene. Moreover, the claim does not specify whether protein or mRNA levels are being measured. Therefore, this rejection of Claims 10-13 is obviated.

The Examiner further alleges that the list of maintenance genes includes proteins having multiple subunits (e.g., ATP synthase), as well as some subunits included in those proteins, thereby allegedly making it unclear as to what molecules are encompassed by the claims. Applicants respectfully disagree. However, for the purpose of expediting the issuance of the claims, Applicants have removed “ATP synthase” from the list of maintenance genes in claim 13.

For the above reasons, the claim rejections under 35 U.S.C. § 112 should be withdrawn.

**C. Claim Rejections under 35 U.S.C. § 103(a)**

Claims 10-13 are rejected under 35 U.S.C. 103(a) as allegedly being unpatentable over MacLeod *et al* in view of Kagawa *et al*. Applicants respectfully disagree.

The Examiner notes that Macleod *et al* do not disclose measuring at least three/five/ten of the maintenance genes recited in claim 13, but alleges that Kagawa *et al* teach “at least ten maintenance genes” that are encompassed by the instant claims as written. Neither reference suggests the limitation(s) encompassed by the claims of the present invention. Moreover, the Examiner has not pointed out any suggestions or motivation to combine the two references and has thus failed to establish a *prima facie* case of obviousness.

Kagawa *et al* discuss ATP synthesis and disclose that although ATP synthase and oligomers supplying energy to  $F_0F_1$  are housekeeping, they are under a coordinated transcriptional control mechanism and their expression may be closely related to cell differentiation (see Abstract, paragraphs 4 and 6). Thus, they may not behave like typical housekeeping genes.

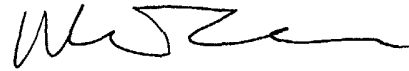
For the above reasons, the claim rejections under 35 U.S.C. § 103(a) should be withdrawn.

### CONCLUSION

For the foregoing reasons, Applicants believe all the pending claims are now in condition for allowance and should be passed to issue. If the Examiner feels that a telephone conference would in any way expedite the prosecution of the application, please do not hesitate to call the undersigned at (408) 731-5000.

The Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment to Deposit Account 01-0431.

Respectfully submitted,



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## APPENDIX A

### VERSION WITH MARKINGS TO SHOW CHANGES MADE TO THE CLAIMS

13. A method for [comparing] determining the expression of a gene in a plurality of biological samples comprising:

measuring the expression of said gene and simultaneously measuring the expression of at least [three] ten maintenance genes selected from the group consisting of: Profilin, Thymosin beta-4 mRNA, Prothymosin alpha[,] mRNA (ProT-alpha), Actin depolymerizing factor, Adducin gamma subunit, Myosin regulatory light chain, Non-muscle type cofilin, Myeloid cell differentiation protein (MCL1), ATP synthase subunit c encoded by P1, ATP synthase alpha subunit, Vacuolar ATP synthase subunit AC45 precursor, ATP synthase gamma-subunit (L-type), ATP synthase beta subunit, Mitochondrial ATPase coupling factor 6 subunit (ATP5A), NaK-ATPase beta-1 subunit, Sodium/potassium-transporting ATPase beta-3 subunit, H+-ATP synthase subunit b, ATP-citrate lyase, [ATP synthase], Vacuolar-type H(+)-ATPase 115 kDa subunit, AQP3 aquaporine 3 (water channel), and Voltage-dependent anion channel isoform 1 (VDAC); and comparing said expression of said gene in said plurality of samples [using] with the expression of said at least [three] ten maintenance genes.

## CLEAN VERSION OF CURRENTLY PENDING CLAIMS

13. A method for determining the expression of a gene in a plurality of biological samples comprising:

measuring the expression of said gene and simultaneously measuring the expression of at least ten maintenance genes selected from the group consisting of:

Profilin, Thymosin beta-4 mRNA, Prothymosin alpha mRNA (ProT-alpha), Actin depolymerizing factor, Adducin gamma subunit, Myosin regulatory light chain, Non-muscle type cofilin, Myeloid cell differentiation protein (MCL1), ATP synthase subunit c encoded by P1, ATP synthase alpha subunit, Vacuolar ATP synthase subunit AC45 precursor, ATP synthase gamma-subunit (L-type), ATP synthase beta subunit, Mitochondrial ATPase coupling factor 6 subunit (ATP5A), NaK-ATPase beta-1 subunit, Sodium/potassium-transporting ATPase beta-3 subunit, H<sup>+</sup>-ATP synthase subunit b, ATP-citrate lyase, Vacuolar-type H(+)-ATPase 115 kDa subunit, AQP3 aquaporine 3 (water channel), and Voltage-dependent anion channel isoform 1 (VDAC);

and comparing said expression of said gene in said plurality of samples with the expression of said at least ten maintenance genes.

12. The method of claim 13 wherein said comparing comprises calculating expression ratio of said gene over said maintenance genes.